DOCKET 5998T260

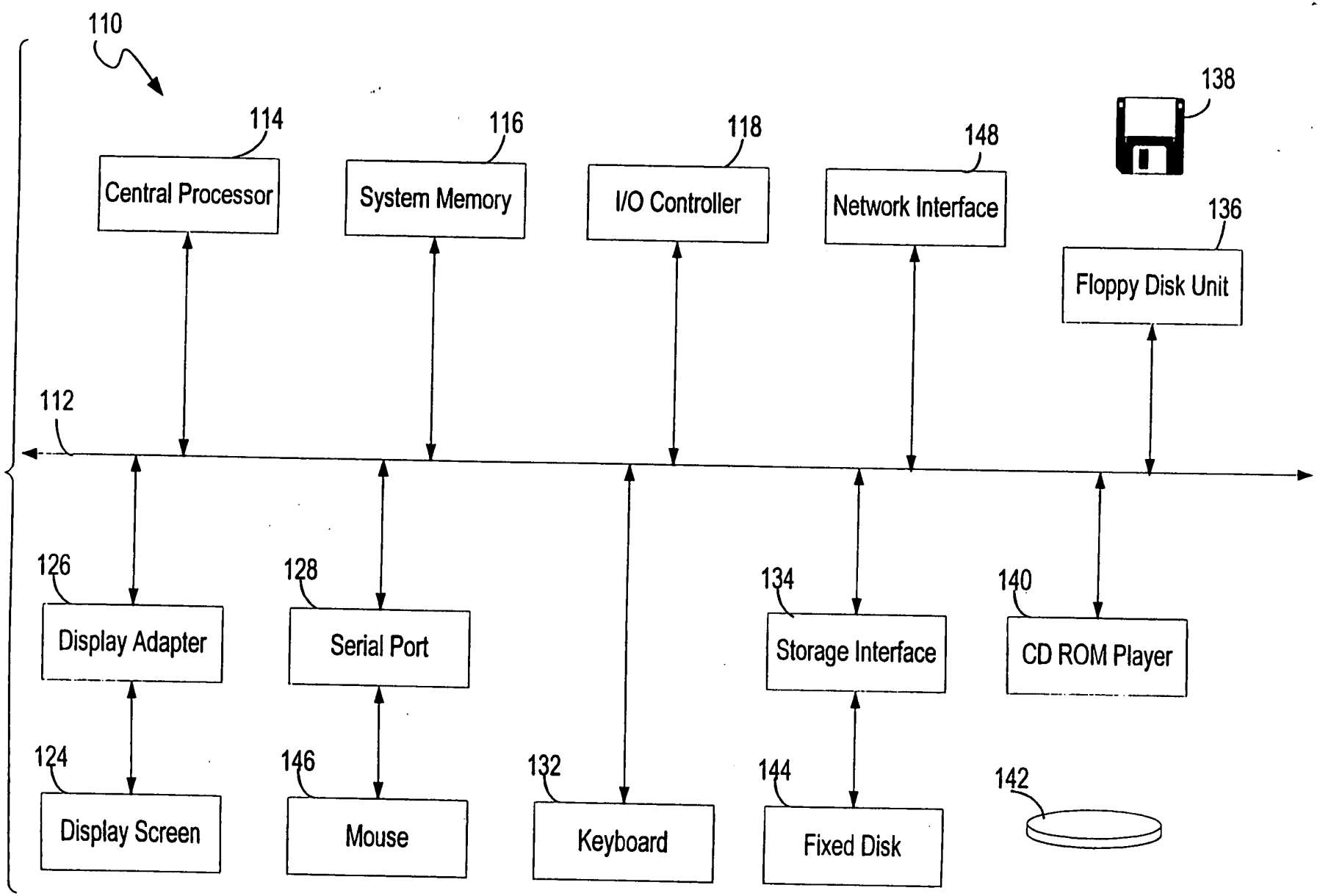


Fig. 1

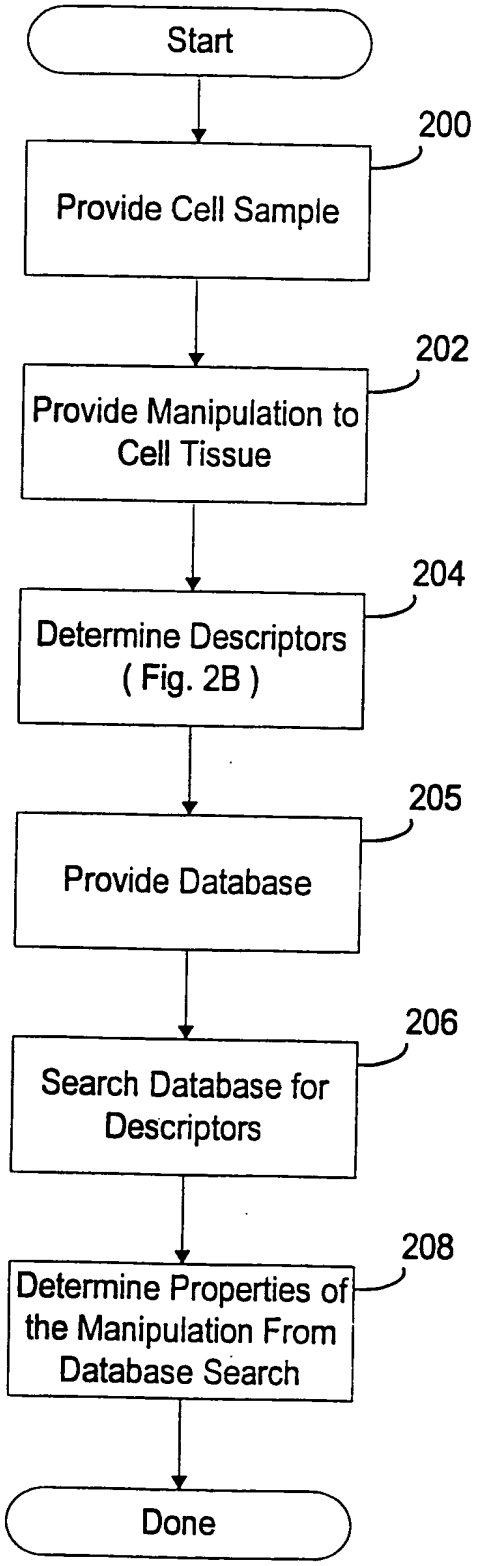

Start
200
Provide Cell Sample
202
Provide Manipulation to Cell Tissue
204
Determine Descriptors (Fig. 2B)
205
Provide Database
206
Search Database for Descriptors
208
Determine Properties of the Manipulation From Database Search
Done

Fig. 2A

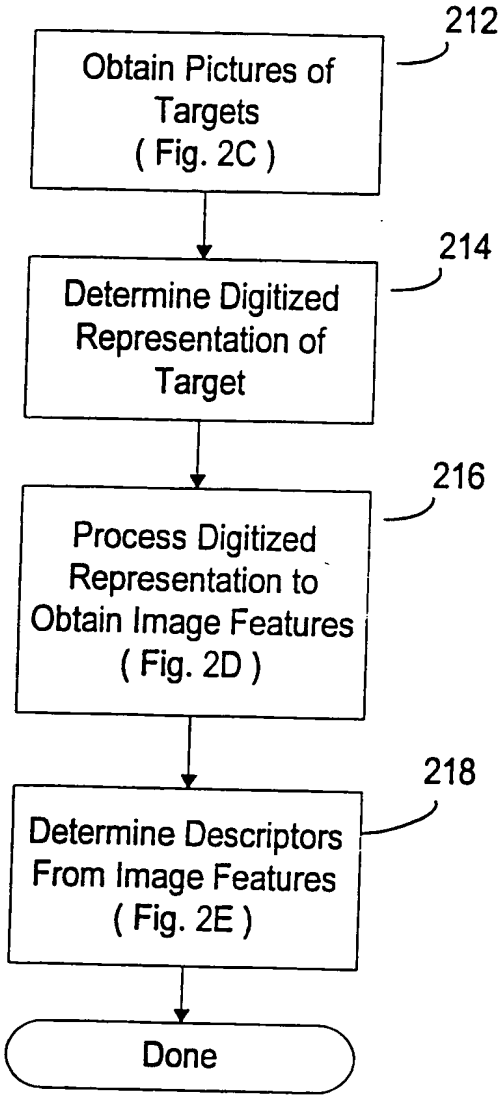


Fig. 2B
Step 204 of Fig. 2A

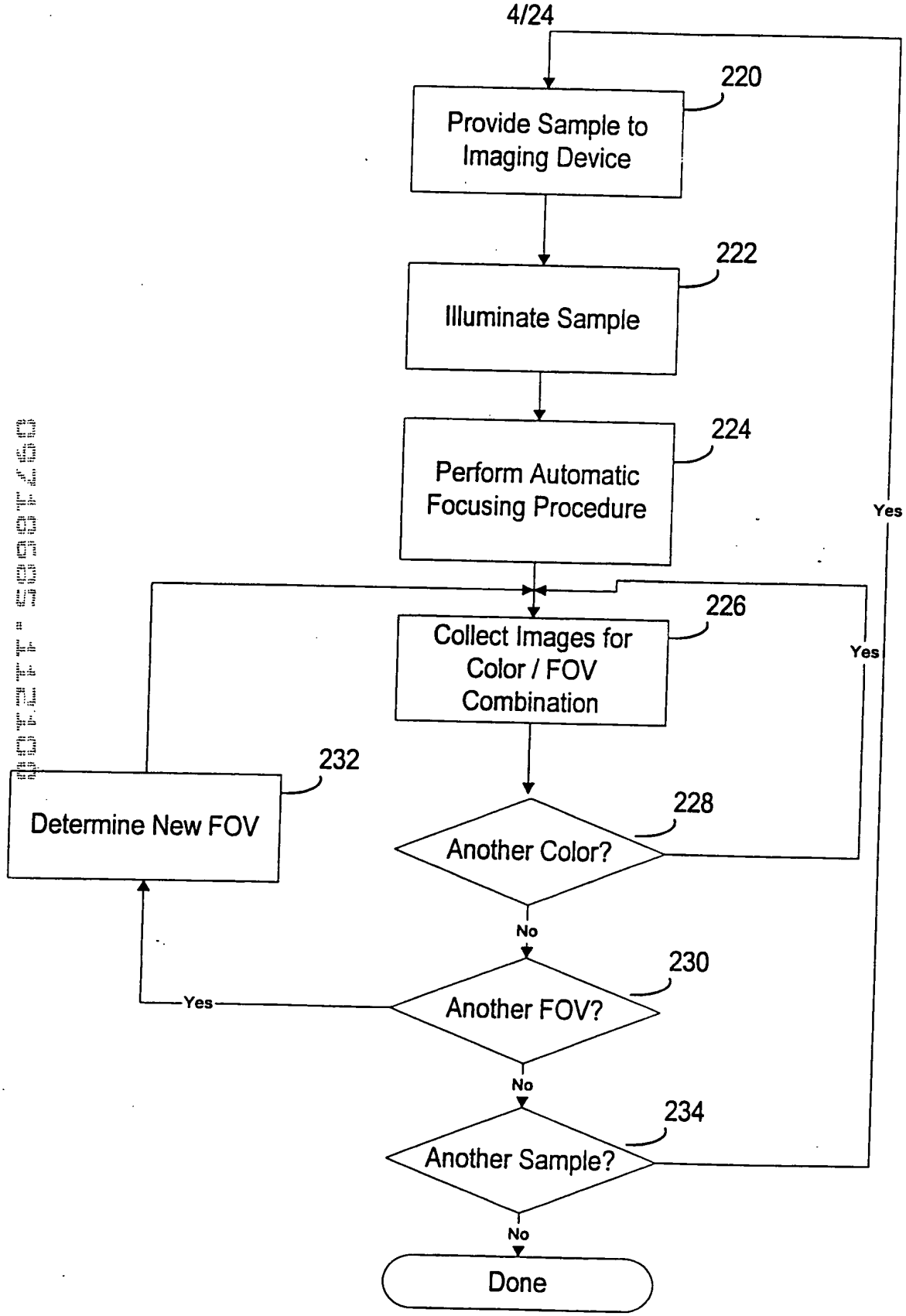


Fig. 2C
Step 214 of Fig. 2B

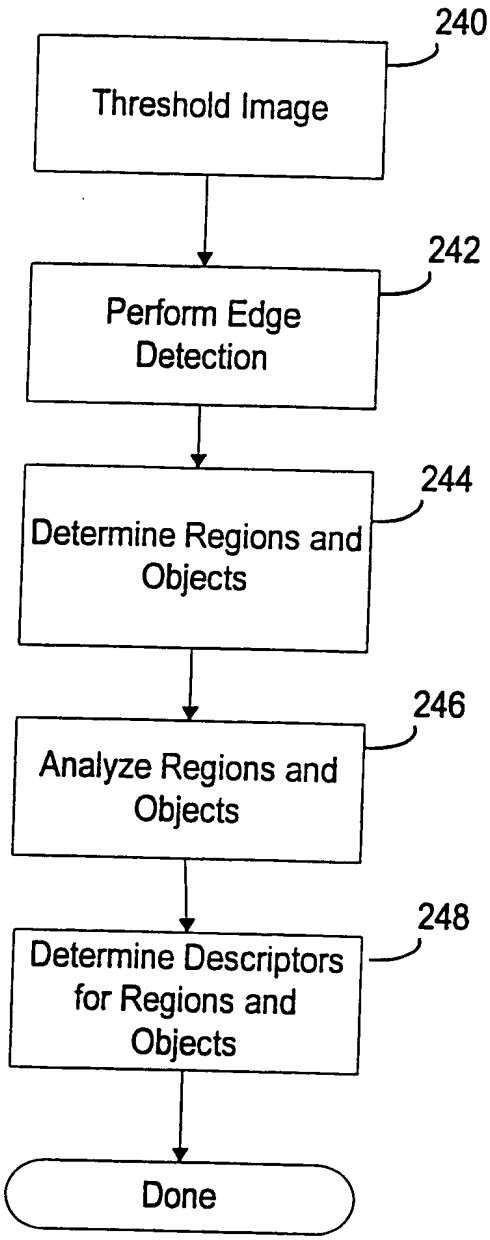


Fig. 2D
Step 216 of Fig. 2B

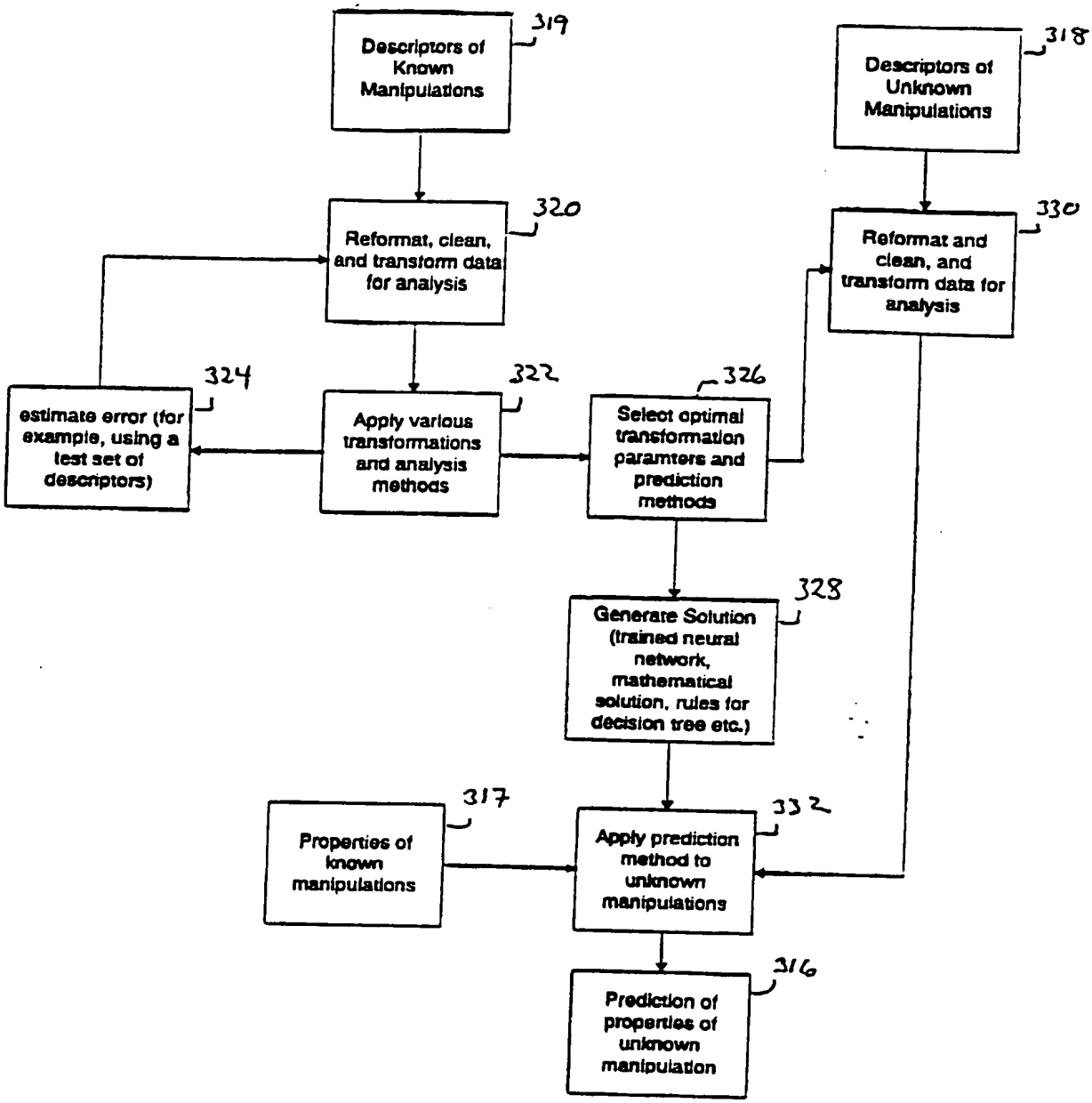

Descriptors of Known Manipulations
319
Descriptors of Unknown Manipulations
318
Reformat, clean, and transform data for analysis
320
Reformat and clean, and transform data for analysis
330
estimate error (for example, using a test set of descriptors)
324
Apply various transformations and analysis methods
322
Select optimal transformation paramters and prediction methods
326
Generate Solution (trained neural network, mathematical solution, rules for decision tree etc.)
328
Properties of known manipulations
317
Apply prediction method to unknown manipulations
332
Prediction of properties of unknown manipulation
316

FIG 2E

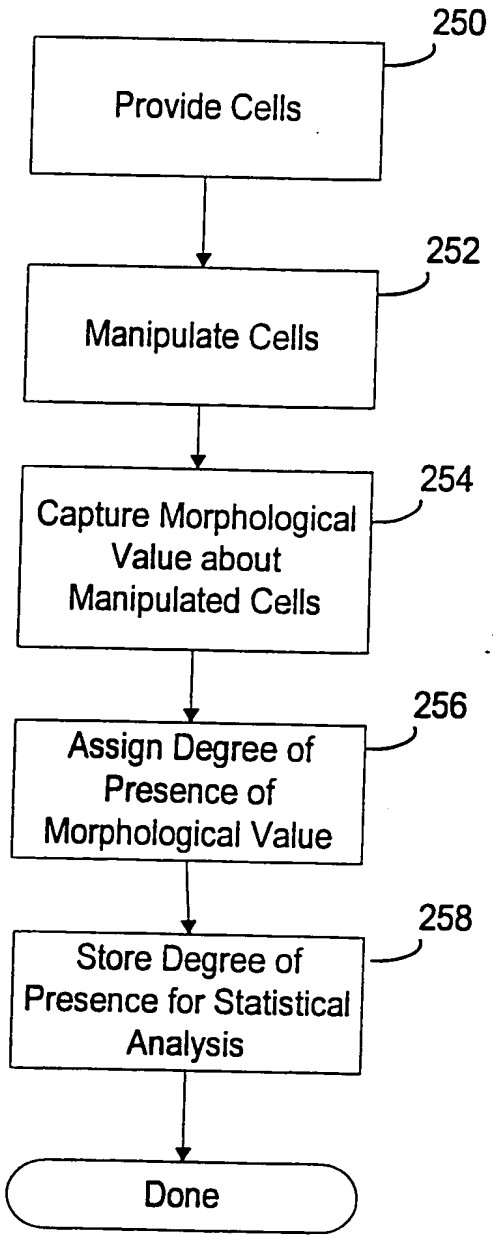

250
Provide Cells
252
Manipulate Cells
254
Capture Morphological Value about Manipulated Cells
256
Assign Degree of Presence of Morphological Value
258
Store Degree of Presence for Statistical Analysis
Done

Fig. 2F

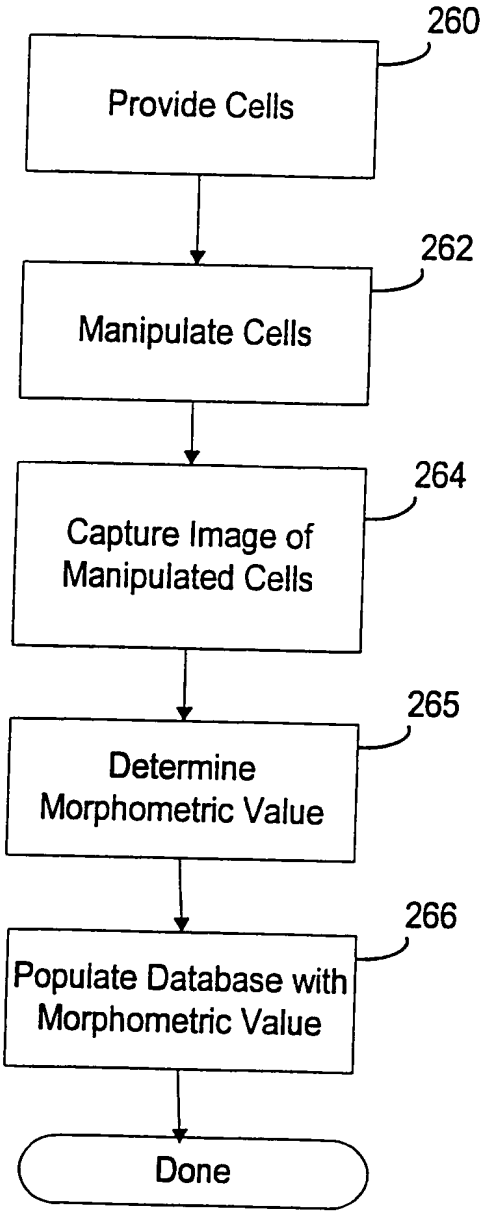

260
Provide Cells
262
Manipulate Cells
264
Capture Image of Manipulated Cells
265
Determine Morphometric Value
266
Populate Database with Morphometric Value
Done

Fig. 2G

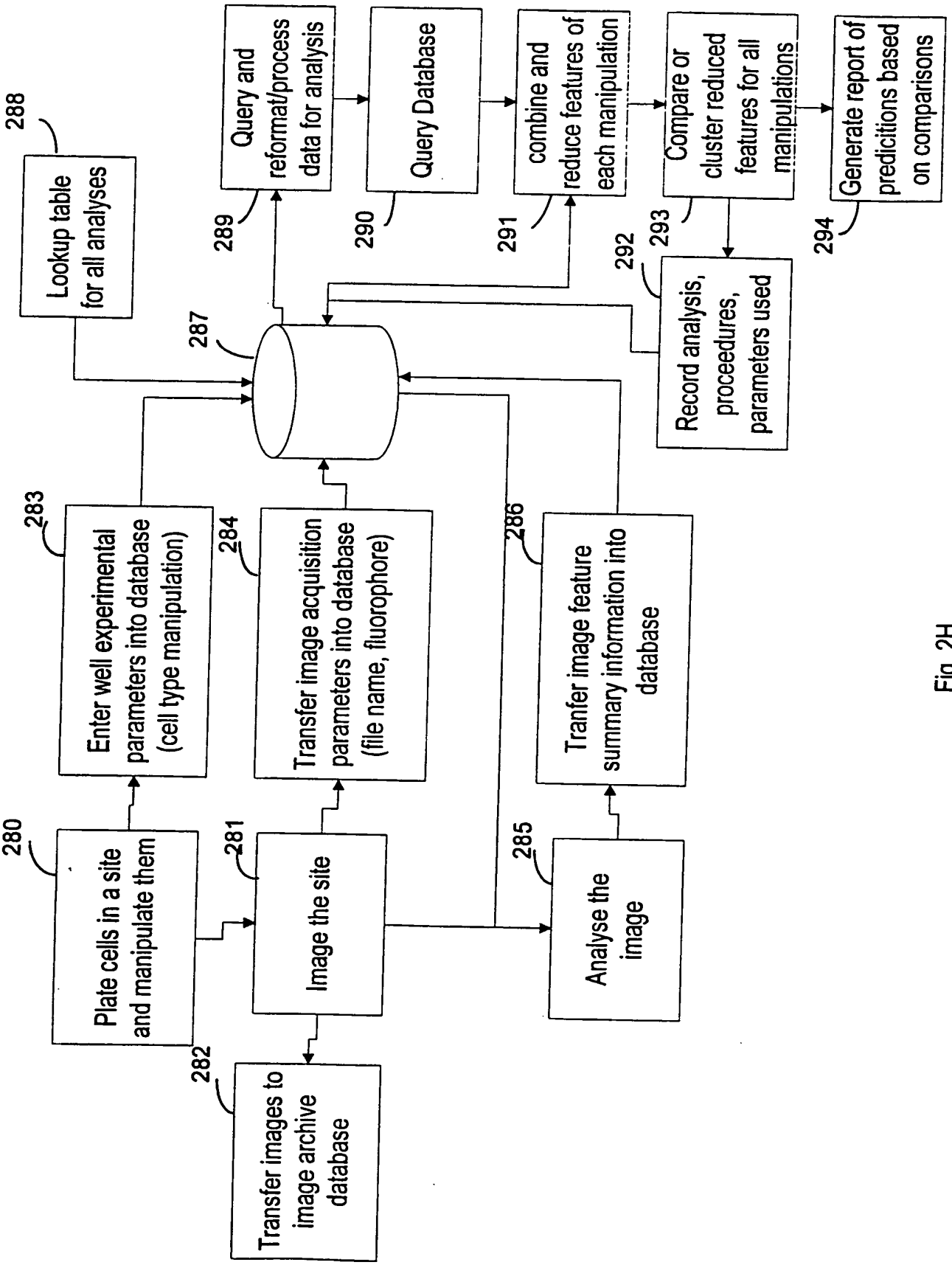

Plate cells in a site and manipulate them
280
Image the site
281
Transfer images to image archive database
282
Enter well experimental parameters into database (cell type manipulation)
283
Transfer image acquisition parameters into database (file name, fluorophore)
284
Tranfer image feature summary information into database
286
Analyse the image
285
Lookup table for all analyses
288
287
Query and reformat/process data for analysis
289
Query Database
290
combine and reduce features of each manipulation
291
Compare or cluster reduced features for all manipulations
293
Record analysis, proceedures, parameters used
292
Generate report of predicitions based on comparisons
294

Fig. 2H

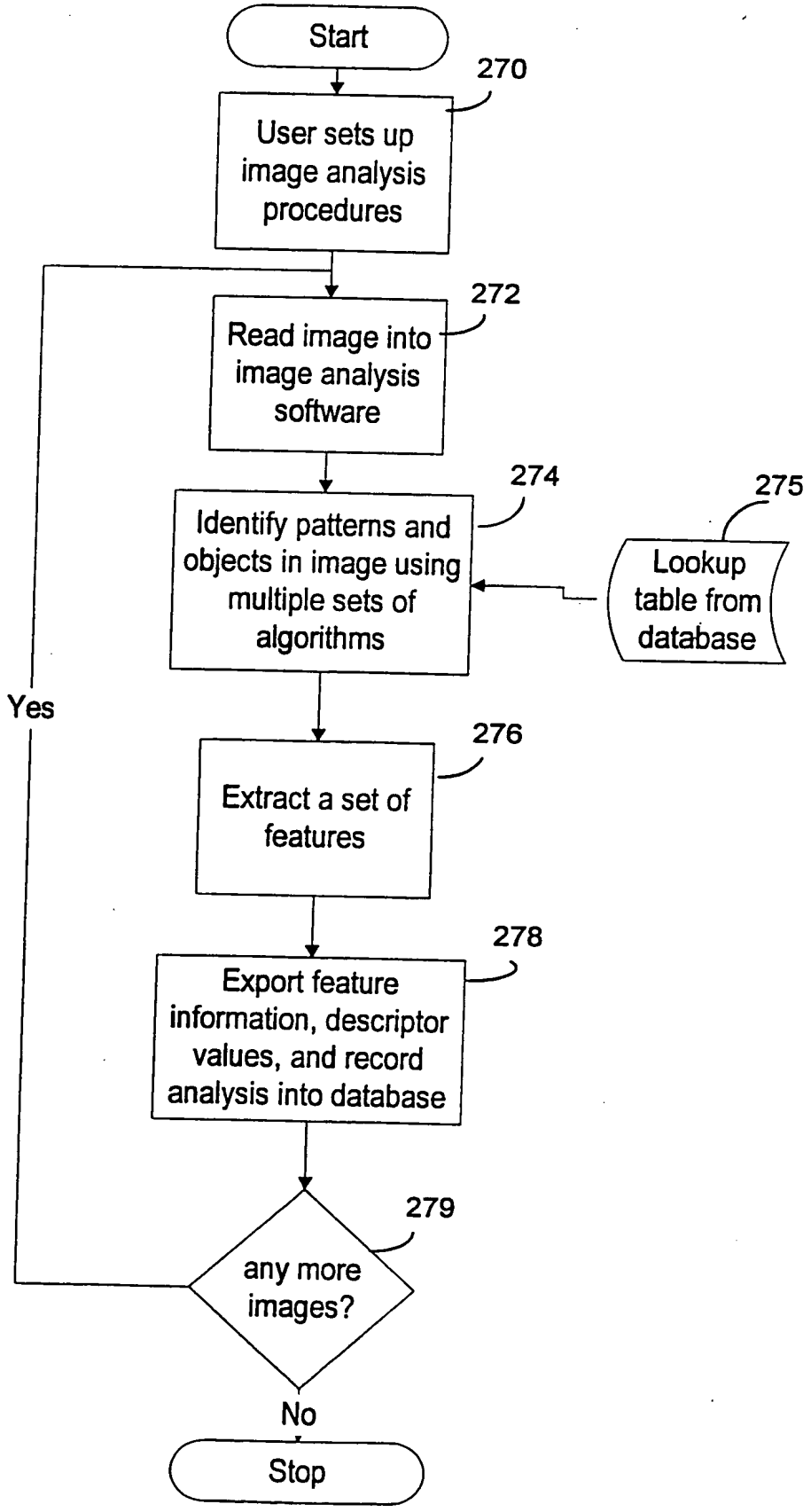

Start
270
User sets up image analysis procedures
272
Read image into image analysis software
274
Identify patterns and objects in image using multiple sets of algorithms
275
Lookup table from database
276
Extract a set of features
278
Export feature information, descriptor values, and record analysis into database
279
any more images?
Yes
No
Stop

Fig. 2I

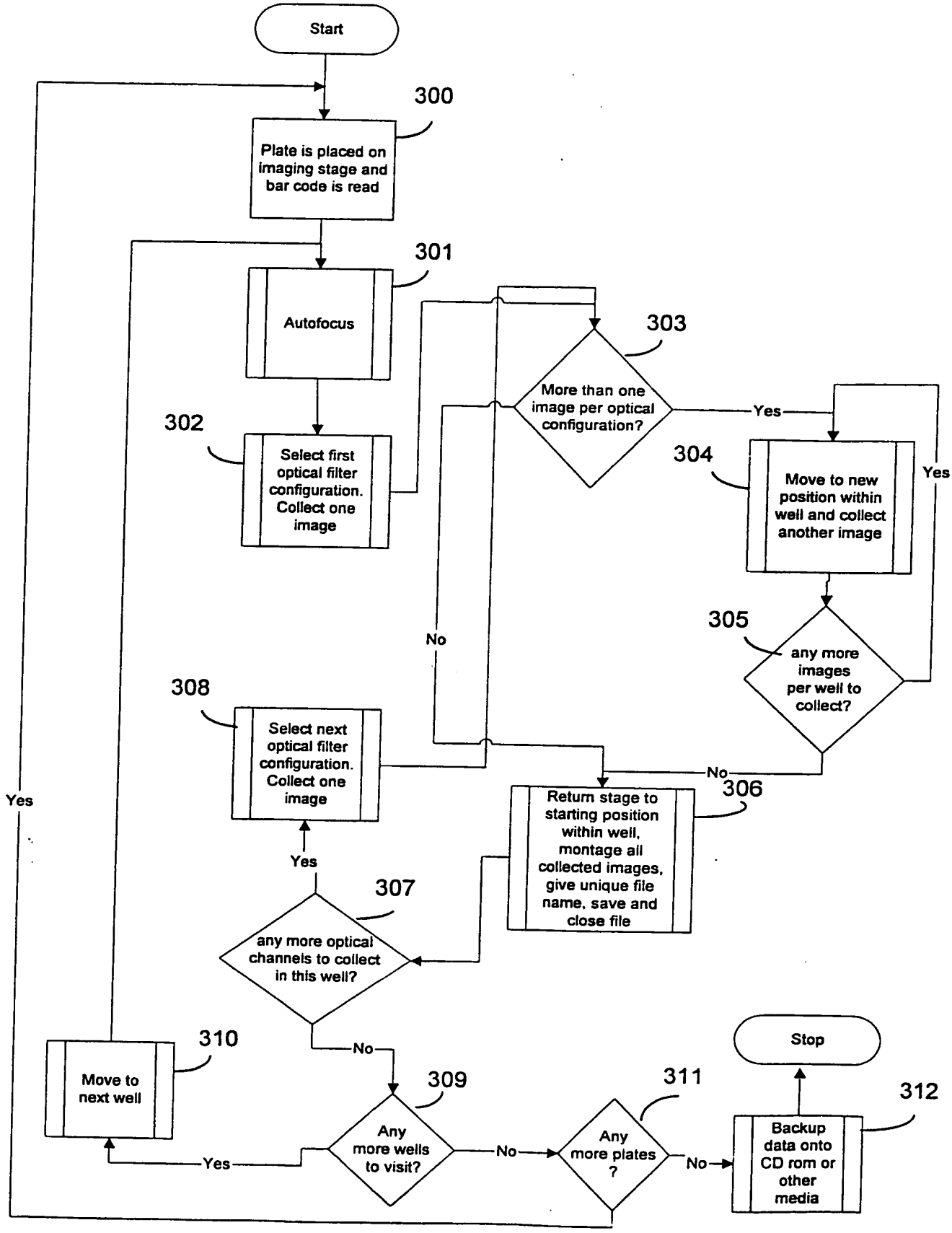

Start
300
Plate is placed on imaging stage and bar code is read
301
Autofocus
302
Select first optical filter configuration. Collect one image
303
More than one image per optical configuration?
Yes
304
Move to new position within well and collect another image
Yes
305
any more images per well to collect?
No
308
Select next optical filter configuration. Collect one image
No
306
Return stage to starting position within well, montage all collected images, give unique file name, save and close file
Yes
307
any more optical channels to collect in this well?
Yes
No
310
Move to next well
309
Any more wells to visit?
Yes
No
311
Any more plates ?
No
312
Backup data onto CD rom or other media
Stop
Yes

Fig. 2J

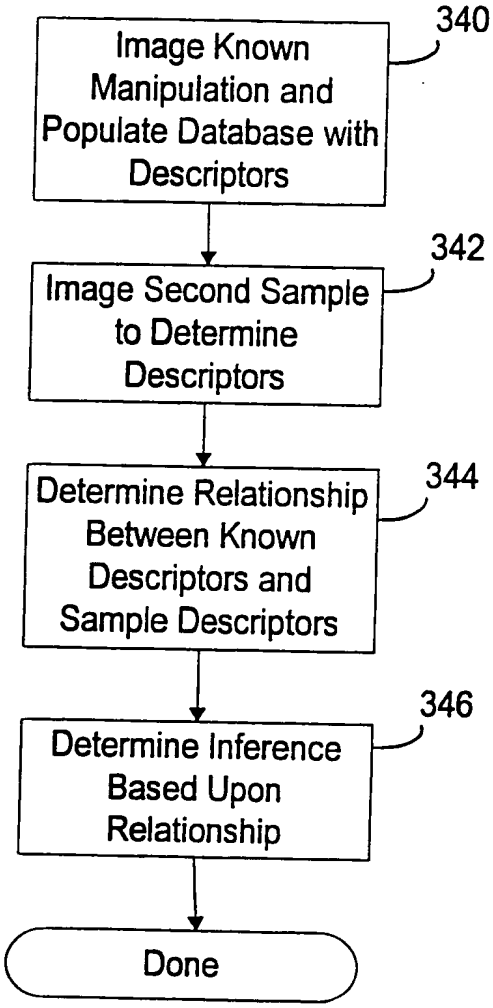

Image Known Manipulation and Populate Database with Descriptors
340
Image Second Sample to Determine Descriptors
342
Determine Relationship Between Known Descriptors and Sample Descriptors
344
Determine Inference Based Upon Relationship
346
Done

Fig. 2K

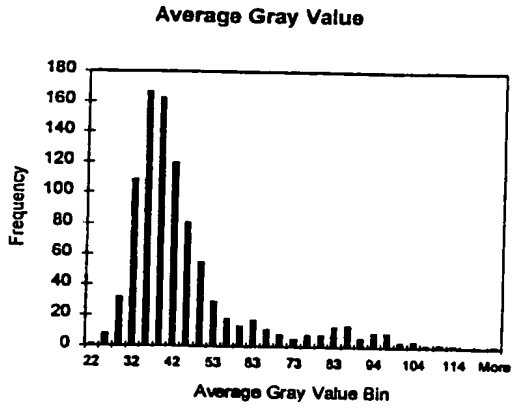


Fig. 3A

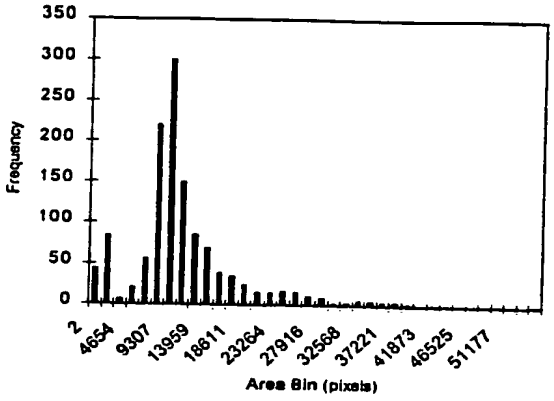


Fig. 3B

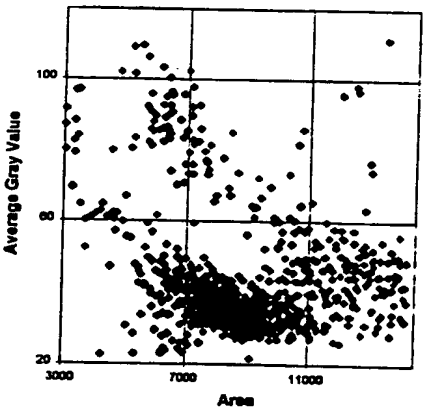


Fig. 3C

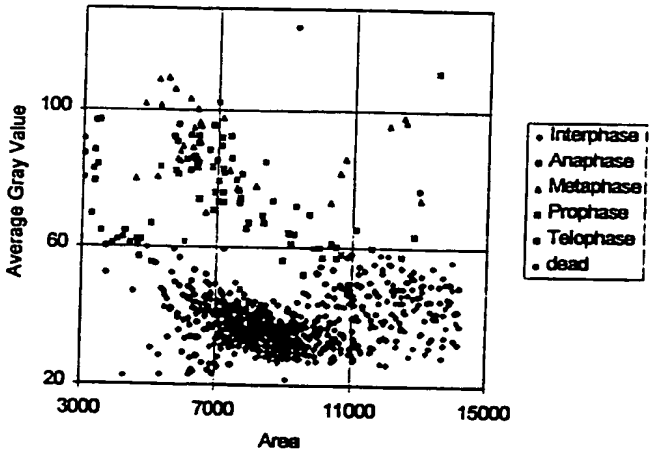


Fig. 3D

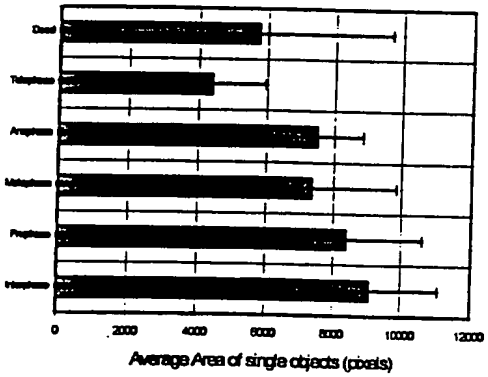


Fig. 3E

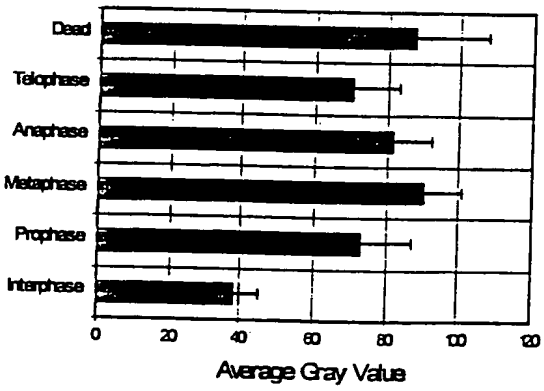
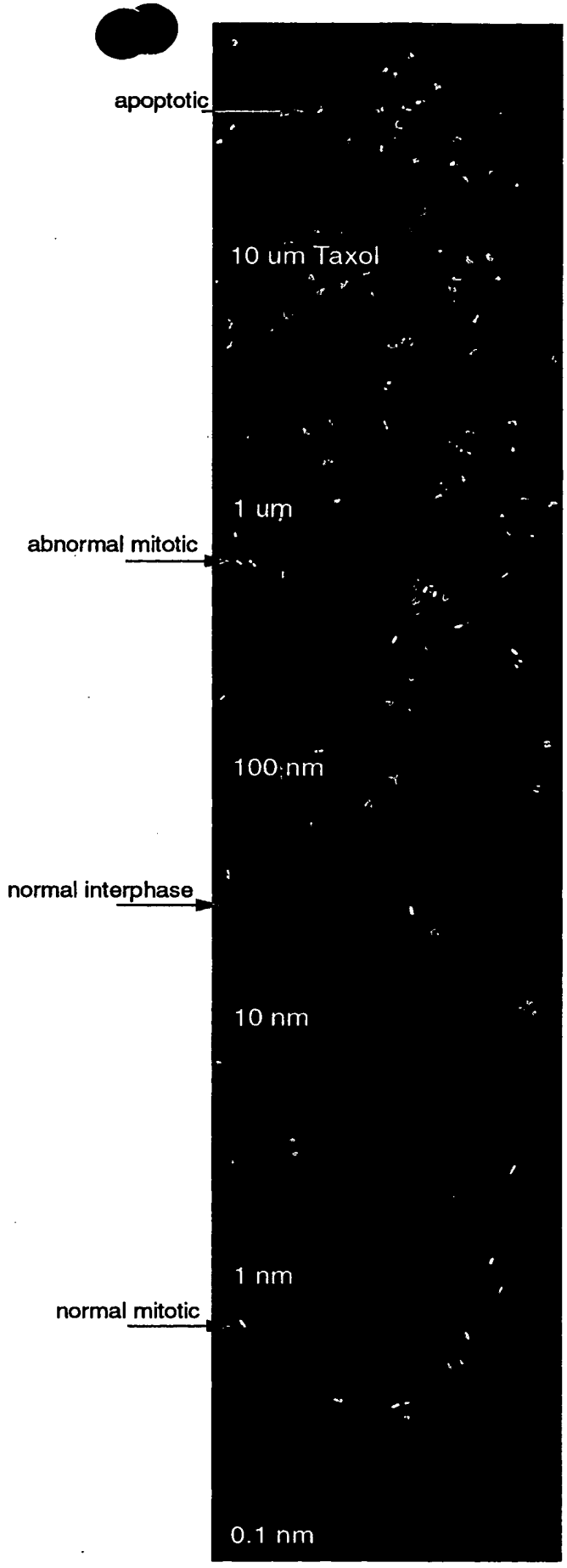


Fig. 3F

FIG. 4



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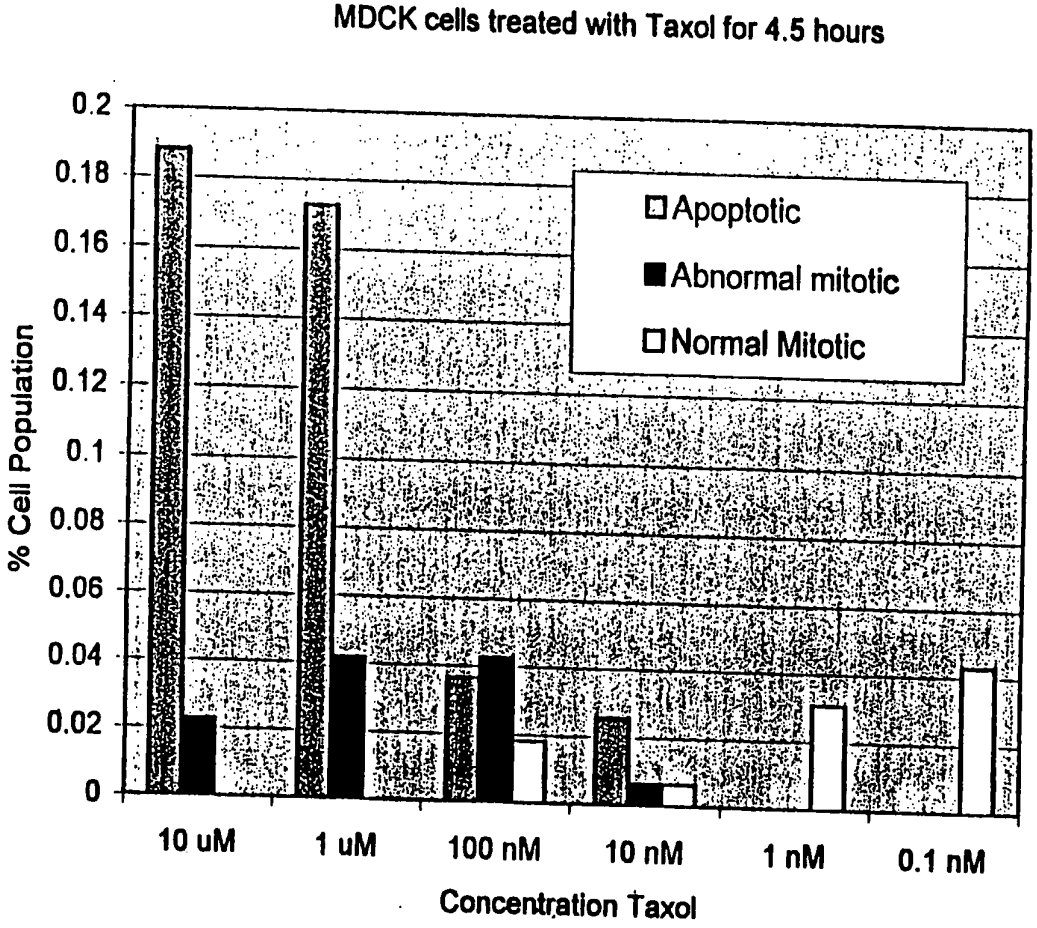

MDCK cells treated with Taxol for 4.5 hours
% Cell Population
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
Apoptotic
Abnormal mitotic
Normal Mitotic
10 uM
1 uM
100 nM
10 nM
1 nM
0.1 nM
Concentration Taxol

Fig. 5

30T3TF'S99ST2S0

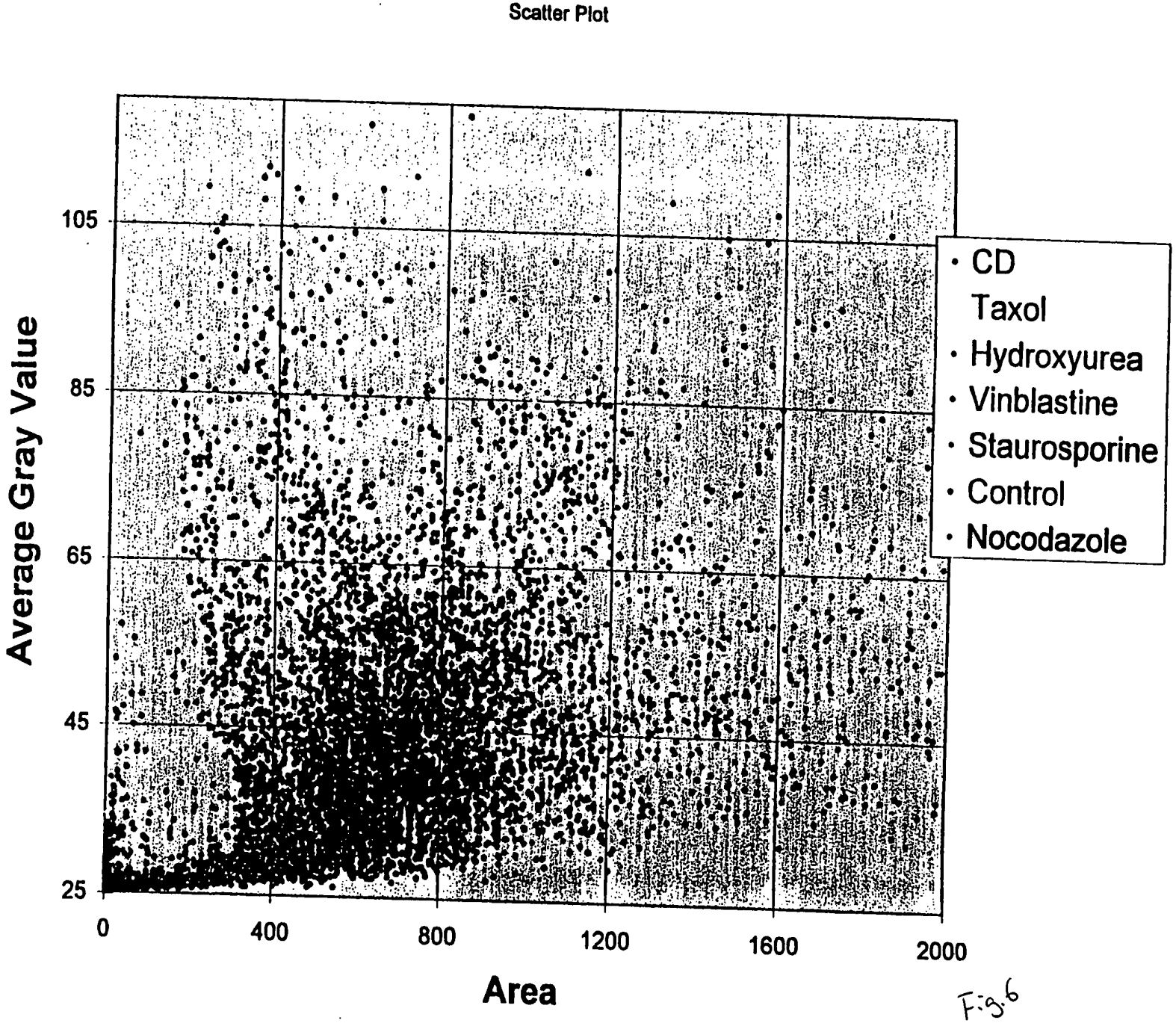


Fig. 6

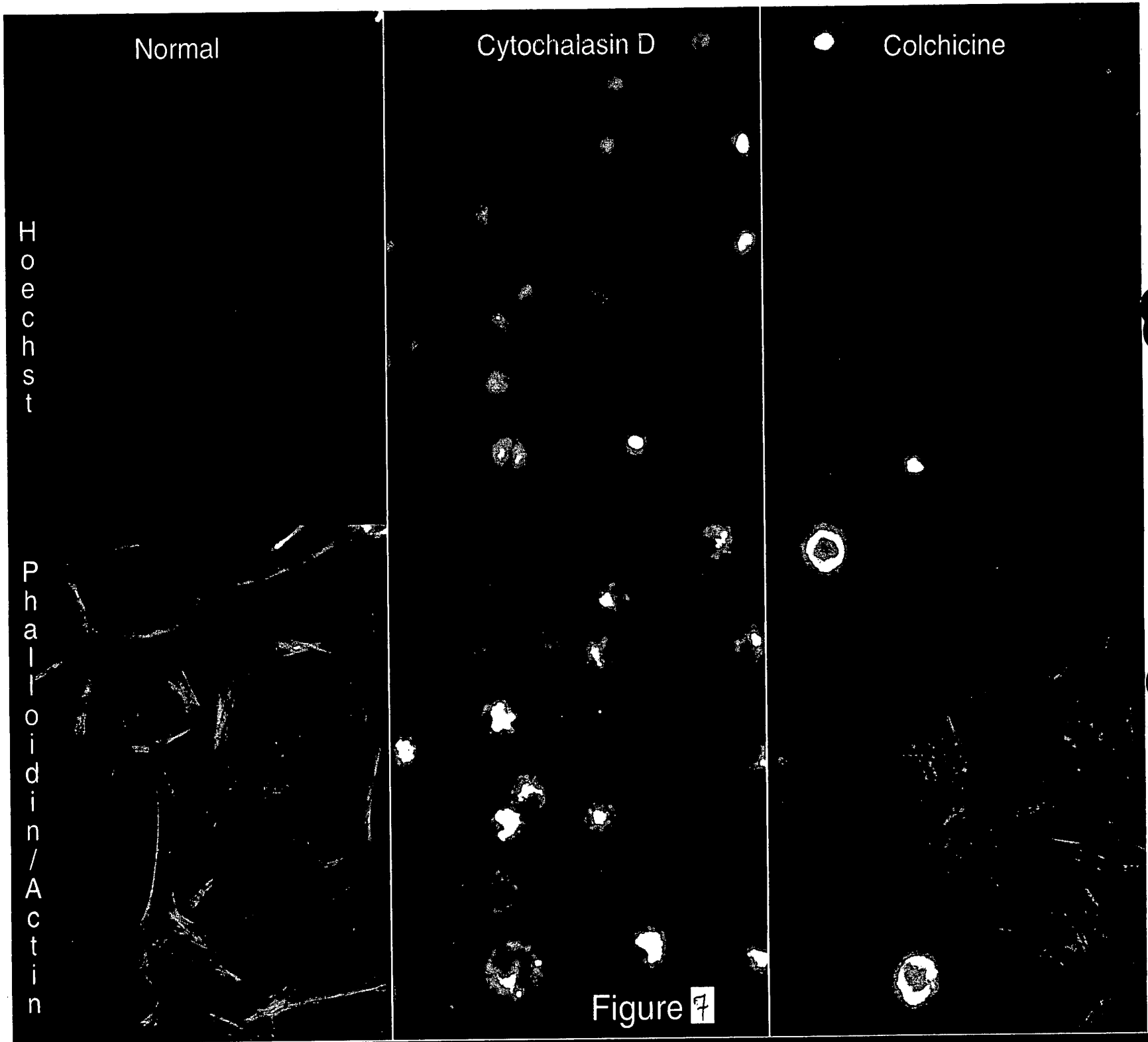

Normal
Cytochalasin D
Colchicine
Hoechst
Phalloidin/Actin

Figure 7

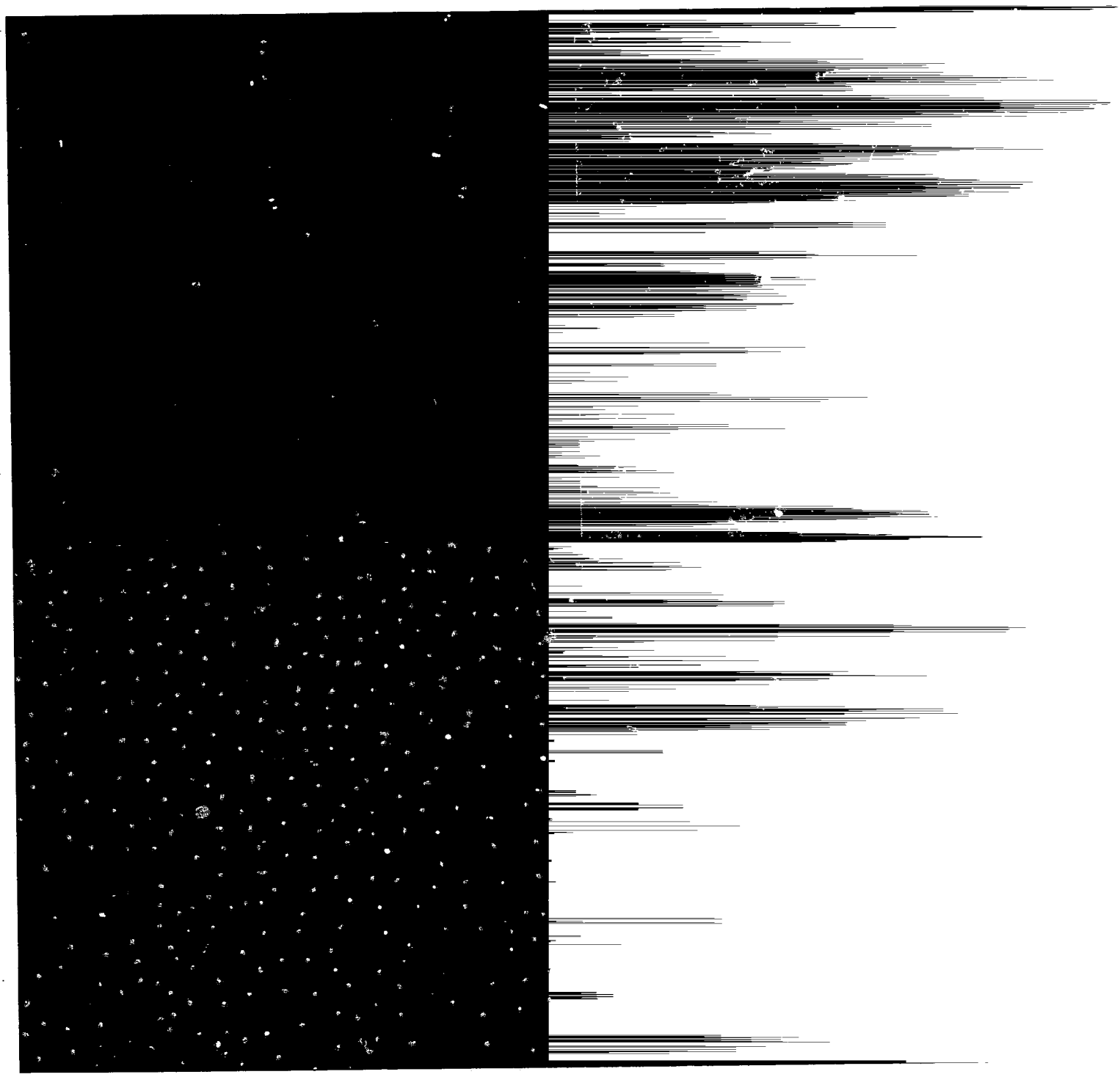


FIG. 8

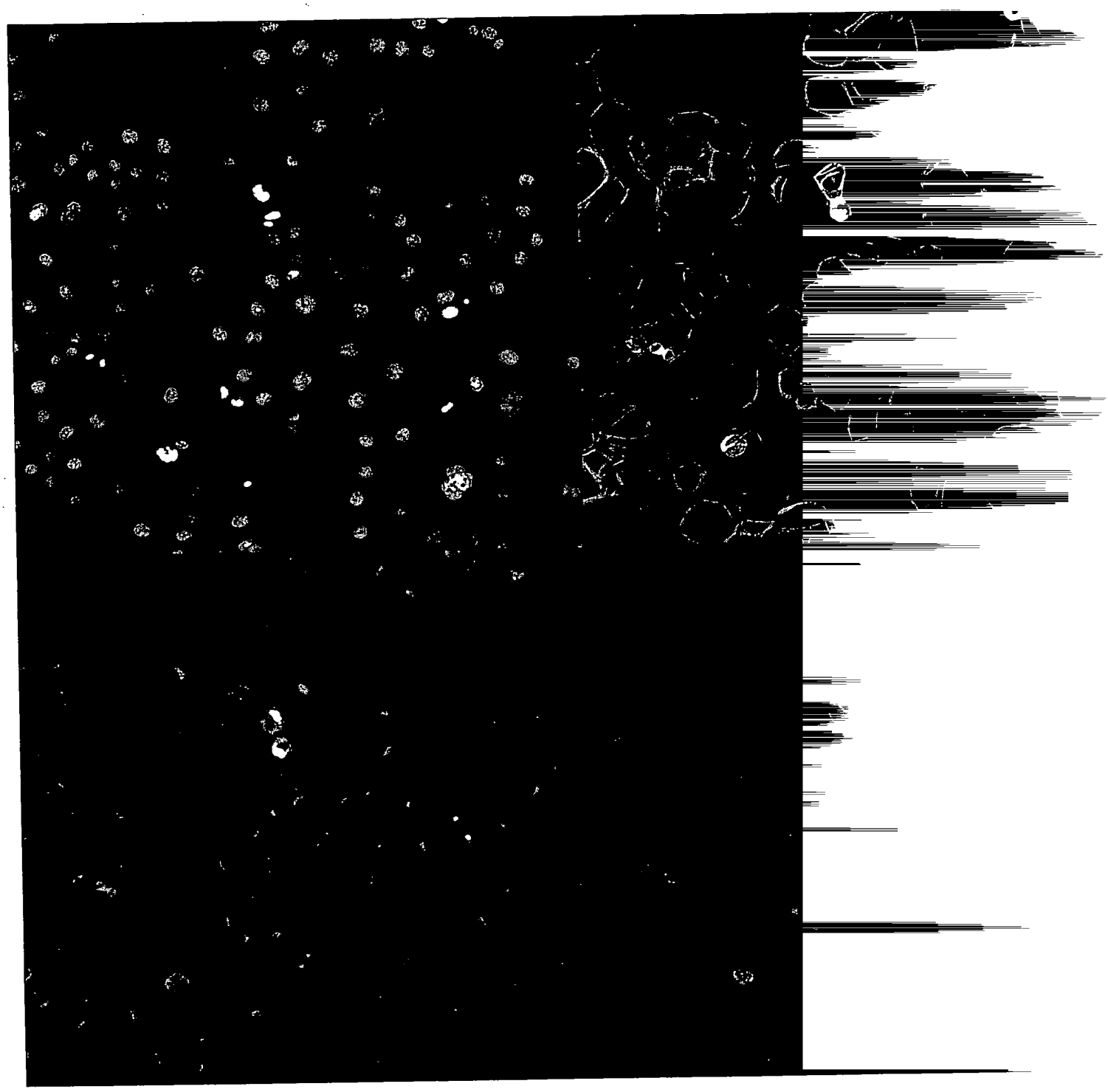


FIG. 9

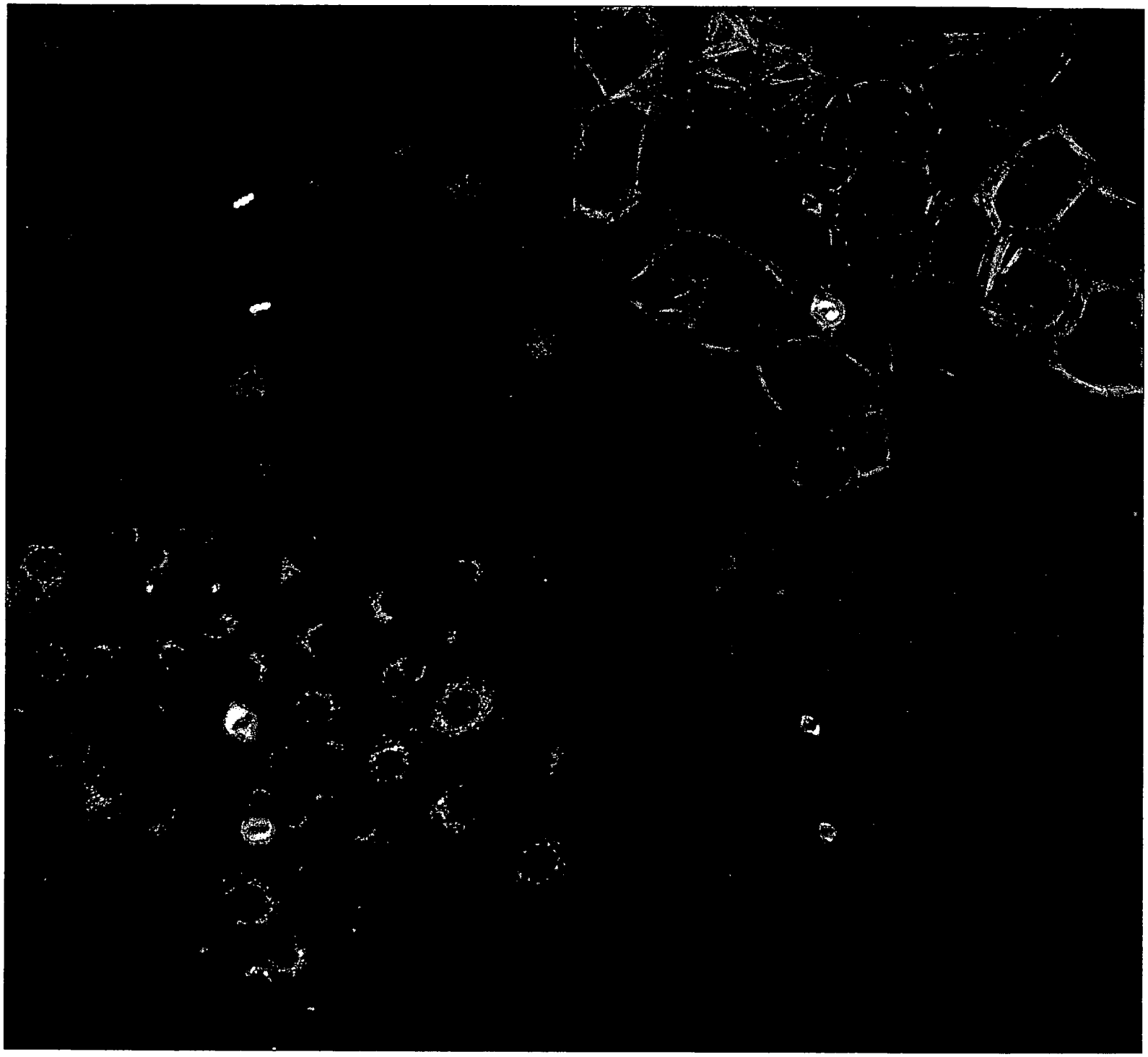


Fig. 10

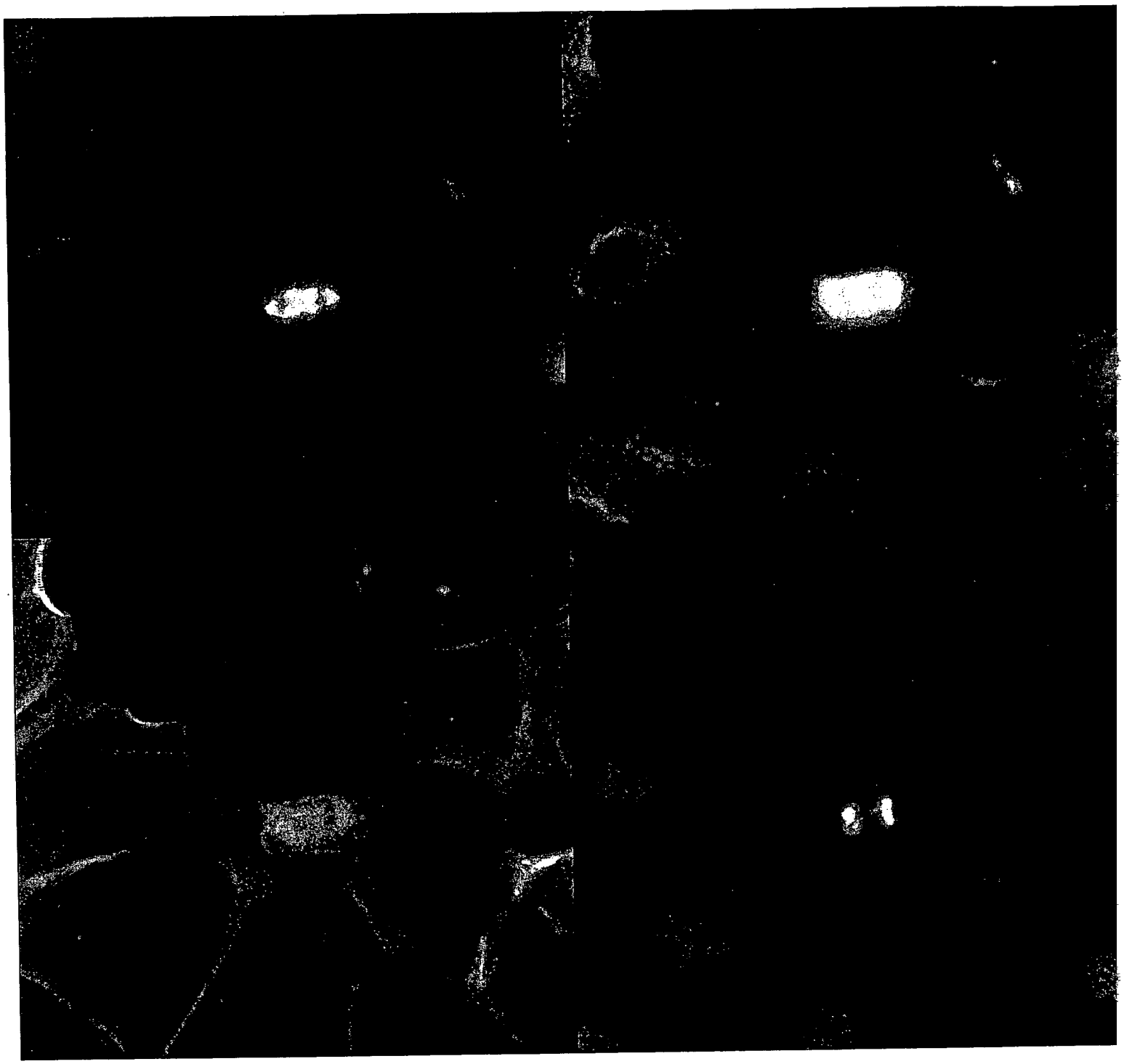


FIG. 11

FIG 12

Conversion of morphometric parameters into nucleic acid code and clustering of the resulting sequences using Neighbor Joining method.

Compound:	Measurements: Count	Area	Perimeter	Length	Breadth	Fiber length	Fiber breadth	Shape factor	Ell. form factor	Inner radius	Outer radius	Mean radius	Equiv. radius	Equiv. sphere vol.	Equiv. prolate vol.	Equiv. oblate vol.	Equiv. sphere surface area	Average gray value	Total gray value	Optical density	Radial dispersion	Texture Difference Moment	EFA Harmonic 2, Semi-Maj	EFA Harmonic 2, Semi-Min
Control	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	a	t	t
Taxol	a	t	t	t	t	t	t	t	a	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t
CD	c	a	a	a	t	a	t	t	c	a	a	a	a	a	a	a	a	t	a	a	a	t	a	g
Nocodozol	c	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t
Staurosporine	g	g	c	a	a	t	a	a	t	g	a	a	a	t	g	g	g	a	a	t	a	t	a	a
Vinblastine	c	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	t	g	t	t	t	t	t
Hydroxyurea	g	t	t	t	t	t	t	g	t	t	t	t	t	t	t	t	t	t	t	c	t	a	t	t

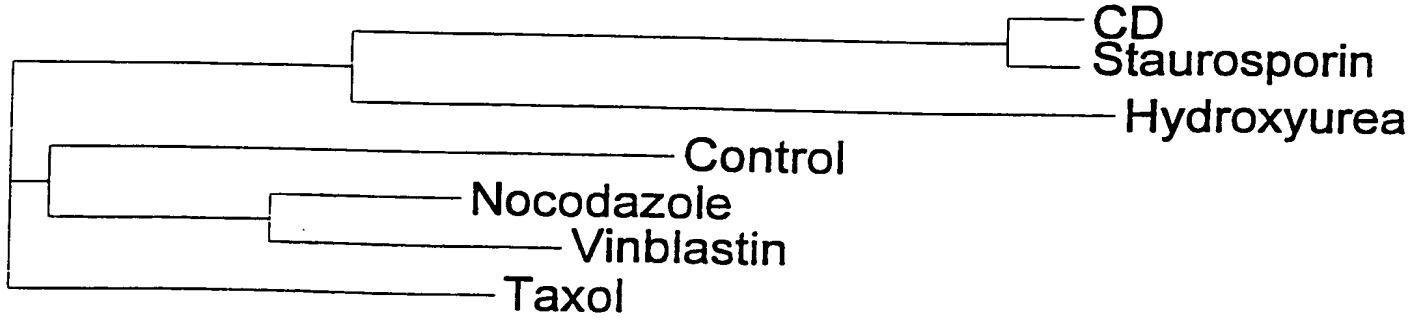


FIG 13

Conversion of morphometric parameters into amino acid codes and clustering of the resulting sequences using Neighbor Joining method.

	Count	Area	Perimeter	Length	Breadth	Fiber length	Fiber breadth	Shape factor	Ell. form factor	Inner radius	Outer radius	Mean radius	Equiv. radius	Equiv. sphere vol.	Equiv. prolate vol.	Equiv. oblate vol.	Equiv. sphere surface a	Average gray value	Total gray value	Optical density	Radial dispersion	Texture Difference Mo	EFA Harmonic 2, Semi-	EFA Harmonic 2, Semi-	
Control	H	P	T	T	N	S	D	W	E	S	T	T	T	F	C	C	P	P	M	C	T	G	T	T	Y
Taxol	G	F	M	M	P	M	P	H	G	S	M	M	W	C	F	P	F	R	C	M	M	H	M	P	S
CD	F	G	G	G	M	G	M	K	A	G	G	G	G	G	G	G	G	H	G	G	G	M	G	V	H
Nocodozol	W	F	M	M	W	M	P	T	R	S	M	M	M	F	M	W	F	M	M	R	M	M	M	F	G
Staurosporine	N	V	A	G	G	M	G	G	Y	V	G	G	G	M	V	V	V	G	G	H	G	M	G	G	V
Vinblastine	F	W	W	M	W	W	C	W	D	S	M	W	W	M	M	M	W	M	V	E	M	M	M	F	P
Hydroxyurea	S	H	H	H	H	H	H	V	H	H	H	H	H	H	H	H	H	H	H	A	H	G	H	H	D

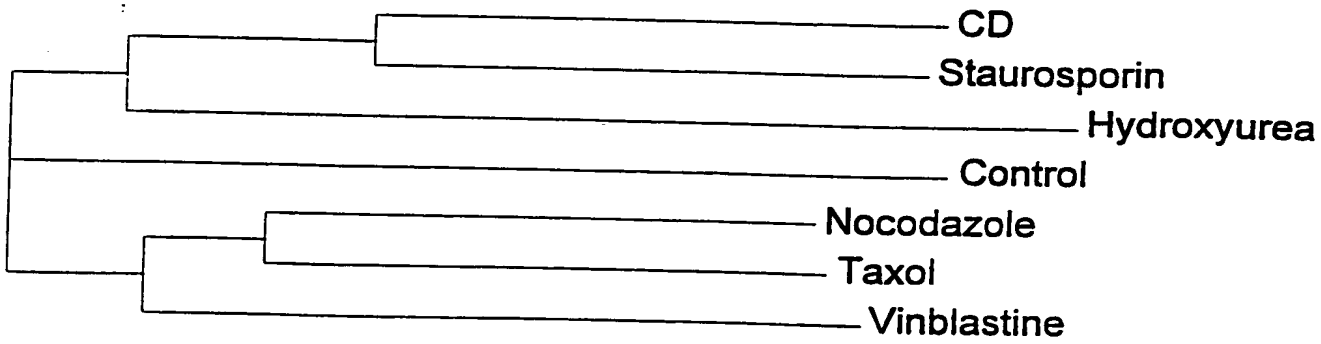


FIG 14